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**CONFIDENTIAL**

Date: February 22, 2010

Pages (including cover): 4

**TO:**Recipient Name

Examiner Lynn Bristol

Firm/Company

U.S. Patent &amp; Trademark Office

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**FROM:** WILLIAM L. WARREN **Email address:** bill.warren@sutherland.com  
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**Message:**

**Re:** U.S. Application No. 10/799,417  
Applicant: Paul A. Krieg  
Title: "METHODS FOR MODULATING ANGIOGENESIS WITH APELIN COMPOSITIONS"  
Our Ref. No.: 20825-0004

Dear Examiner Bristol:

In response to our telephone conference on Friday, February 19<sup>th</sup>, attached please find a revised set of claims. I look forward to speaking with you in the near future.

Regards,



William L. Warren  
Reg. No. 36,714

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U.S. Utility Patent Application Serial No. 10/799,417 entitled,  
"METHODS FOR MODULATING ANGIOGENESIS WITH APELIN COMPOSITIONS"

**PROPOSED AMENDMENTS AS OF FEB 23, 2010**  
**FOR DISCUSSION ONLY – DO NOT ENTER**

1. (Currently Amended) A method of inhibiting angiogenesis in a patient in need thereof ~~biological sample~~, comprising
  - a. ~~providing a biological sample; and~~
  - b. ~~combining the biological sample in vivo with~~ administering to the patient an angiogenesis-inhibiting amount of a composition comprising ~~an inhibitor of~~ apelin activity an anti-apelin antibody or fragment thereof that binds apelin polypeptide of SEQ ID NO:4 and inhibits angiogenesis, wherein the angiogenesis is characterized by in vivo generation of a new blood vessel from an existing blood vessel.
- 2.-4. (Canceled)
5. (Original) The method of Claim 1, wherein the composition further comprises an anti-cancer agent and wherein the anti-cancer agent is selected from the group consisting of a chemotherapeutic agent, a radiotherapeutic agent, an anti-angiogenesis agent, and an apoptosis-inducing agent.
6. (Previously Presented) The method of Claim 5, wherein the composition comprises an anti-angiogenesis agent that inhibits an angiogenic factor selected from the group consisting of VEGF (VEGF-A), VEGF-B, VEGF-C, VEGF-D, VEGF-E, PlGF, acidic fibroblast growth factor (FGF-1), basic fibroblast growth factor (FGF-2), PDGFB, EGF, LPA, HGF, PD-ECP, IL-8, angiogenin, TNF-alpha, TGF-beta, TGF-alpha, proliferin, and PLGF.
- 7.-20. (Canceled)

21. (Original) The method of Claim 1, wherein the composition comprises a pharmaceutically acceptable carrier.
22. (Currently Amended) The method of Claim 1, wherein the patient is a mammal  
~~biological sample is a mammalian biological sample.~~
23. (Currently Amended) The method of Claim 1, wherein the patient is a human  
~~sample is a human biological sample.~~
- 24-25. (Canceled)
26. (Currently Amended) The method of Claim 1, wherein the patient has a disease or condition involving angiogenesis.
27. (Canceled)
28. (Currently Amended) The method of Claim 24, further comprising  
e. administering to the patient a therapeutically effective amount of an anti-cancer agent,  
wherein the anti-cancer agent is selected from the group consisting of a chemotherapeutic agent, a radiotherapeutic agent, an anti-angiogenic agent, and an apoptosis-inducing agent.
29. (Original) The method of Claim 28, wherein the anti-cancer agent is an anti-angiogenic agent.
30. (Previously Presented) The method of Claim 28, wherein the anti-angiogenic agent is an inhibitor of an angiogenic factor selected from the group consisting of VEGF (VEGF-A), VEGF-B, VEGF-C, VEGF-D, VEGF-E, PlGF, acidic fibroblast growth factor (FGF-1), basic fibroblast growth factor (FGF-2), PDGFB, EGF, LPA, HGF, PD-ECF, IL-8, angiogenin, TNF-alpha, TGF-beta, TGF-alpha, proliferin, and PLGF.
- 31.-59. (Canceled)

60. (New) A method of inhibiting angiogenesis in a biological sample, comprising contacting the biological sample with an angiogenesis-inhibiting amount of a composition comprising an anti-apelin antibody or fragment thereof that binds the apelin polypeptide of SEQ ID NO:4 and inhibits angiogenesis, wherein the angiogenesis is characterized by *in vivo* generation of a new blood vessel from an existing blood vessel.
61. (New) The method of Claim 60, wherein the biological sample is a mammalian biological sample.
62. (New) The method of Claim 60, wherein the biological sample is a human biological sample.